

REMARKS

Applicant thanks the Examiner for the thorough review of the application and claims. Prior to this amendment, claims 49, 50, 55-64, 69-78, 80, 90, 95, 97 and 98 were pending. Claims 50, 55-57, 63, 64 and 69-72 have been canceled herein without prejudice. Applicants respectfully reserve the right to file one or more continuation and/or divisional applications with claims directed to the subject matter encompassed by the canceled claims.

Claim 49 has been amended. Supported for the amendment may be found throughout the specification, particularly at pages 53 and 54, and in the claims as originally filed. The amendments herein are not to be interpreted as a surrender of any subject matter originally encompassed by the claims.

No new matter has been added by any of the amendments. After entry of this amendment claims 49, 58-62, 73-78, 80, 90, 95, 97 and 98 will be pending.

Objection to the Abstract

The Abstract was objected to as not being descriptive of the instantly claimed invention. Accordingly, Applicant has amended the abstract to more clearly describe the invention.

Rejection under 35 U.S.C §112

Enablement

Claims 49, 50, 55-58, 63, 64, 69-72, 80, 90, 95, 97 and 98 stand rejected under 35 U.S.C. § 112, 1st paragraph on the grounds that the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection contends that while the specification provides enablement for making and using a toxin of SEQ ID NO: 2, 11 or 32 and methods for using said toxins to control insect pests, it does not reasonably provide enablement for toxins produced by expression of a nucleic acid with 95%, 95% or 96% identity to SEQ ID NO: 1 or that hybridizes to nucleotides 1981-2367 of SEQ ID NO: 1, toxins with

91%, 95%, 97% and 99% identity to SEQ ID NO: 2, and toxin comprising only amino acids 661-788 of SEQ ID NO: 2, and to methods of using the toxins to control pests. The rejection asserts further that to make the claimed invention to the full extent of its scope would require undue experimentation. While Applicant maintains that the claims meet the requirements of §112, in the interest of advancing prosecution and without any intention to relinquish any scope of equivalents unforeseeable at the time of this amendment, claims 50, 55-57, 63, 64 and 69-72 have been canceled and claim 49 has been amended. Applicant respectfully submits that the cancellation of claims 50, 55-57, 63, 64, and 69-72 renders the rejection of these claims moot.

The first paragraph of 35 U.S.C. §112 requires that the specification describe how to make and use the claimed subject matter. That requirement has been met in the present application. In particular, the specification describes how to make and use variants of SEQ ID NO: 2 that are active against particularly European corn borer, but also other lepidopteran insects.

The Federal Circuit stated in In re Vaeck that “[E]nablement requires that the specification teach those in the art to make and use the invention without ‘undue experimentation.’ ... That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is ‘undue.’” In re Vaeck, 947 F.2d 488, 495 (Fed. Cir. 1991) (emphasis in original). Some experimentation, even a considerable amount, is not “undue” if, for example, it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. See In re Wands, 858 F.2d 731 (Fed. Cir. 1988).

Claim 49 as amended recites that the isolated toxin (1) comprises an amino acid sequence that has 97% sequence identity to SEQ ID NO: 2 over the entire length of the amino acid sequence, (2) comprises amino acids 661-788 of SEQ ID NO: 2 at its C-terminus and (3) has activity against European corn borer. Amended claim 49 and the claims dependent therefrom are enabled by the instant specification.

The specification discloses a novel vegetative insecticidal protein, Vip3C, as SEQ ID NO: 2. Contrary to the Examiner’s assertion that the instant specification “does not teach which amino acids are responsible for toxicity,” the instant specification clearly identifies a specific C-terminal domain of SEQ ID NO: 2, which comprises amino acids 661-788, that is responsible for toxicity against European corn borer (ECB; *Ostrinia nubilalis*) and diamond back moth (DBM;

Plutella xylostella) (See Example 9, pp. 53-54). The specification further provides guidance for making a variant of Vip3C by moving amino acids 661-788 of SEQ ID NO: 2 (the ECB-active C-terminal domain) to a nonECB-active Vip3 (e.g. Vip3A) and demonstrating that the resulting toxin now has ECB and DBM activity in addition to other lepidopteran insects (See Table 10 at paragraph [00184]). This resulting toxin, the amino acid sequence of which is disclosed as SEQ ID NO: 11, has an amino acid sequence that is 97% identical to SEQ ID NO: 2 over the entire length of the amino acid sequence and has a C-terminus that comprises amino acids 661-788 of SEQ ID NO: 2 as required by claim 49. The specification further provides guidance for isolating Vip3C homologs from *Bacillus* and in fact discloses the sequence of one such embodiment as SEQ ID NO: 32. It was well within the skilled person's purview at the time the instant application was filed to be able to align two or more amino acid sequences and determine their overall percent identity. An example of such an alignment is enclosed as Exhibit A. Exhibit A shows that SEQ ID NO: 11 and SEQ ID NO: 32 have 97% identity and 99% identity to SEQ ID NO: 2, respectively. Thus, the skilled person could determine that the Vip3C homolog disclosed as SEQ ID NO: 32 has 99% identity to SEQ ID NO: 2 as required in dependent claim 58, comprises amino acids 661-788 of SEQ ID NO: 2 at its C-terminus and is active against European corn borer as required by claim 49, from which claim 58 depends.

The Examiner asserts that the amino acids required for toxicity toward different insects appears to be unpredictable. For support, the rejection relies on Selvapandiyani *et al.* (2001, Appl. Environ. Microbiol. 67:5855-5858), which is asserted to teach that a Vip3 protein with three amino acid substitutions affected toxicity towards one insect species [black cutworm] but not others. Applicant respectfully disagrees with this assertion for the following reasons. First, the instant claims require that the toxin variants of claim 49 comprise amino acids 661-788 of SEQ ID NO: 2, which is identified to the skilled person as being the essential structural feature providing functionality of the Vip3C protein against European corn borer. Second, it is not clear from Selvapandiyani *et al.*, as the Examiner asserts, that the three amino acid differences are responsible for the lack of activity of the Vip3S protein against black cutworm. On page 5857, column 2, last paragraph, Selvapandiyani *et al.* state, "*At present, it is difficult to understand the reasons for the observed lack of insecticidal activity against A. ipsilon by VIP described here. Is it due to diversity in A. ipsilon, or are the three different amino acid residues in VIP critical for*

toxicity?” Applicant respectfully submits that given the inconclusive results, Selvapandiyan *et al.* has no bearing on whether the instant claims meet the enablement requirement.

Applicant respectfully submits that by following the teaching of the instant application, it would be routine for the skilled person to make or isolate a Vip3C variant comprising at its C-terminus amino acids 661-788 of SEQ ID NO: 2 and test that variant against European corn borer. The variant Vip3C could easily be aligned with the Vip3C of SEQ ID NO: 2 to determine overall percent identity. Therefore, without undue experimentation, the skilled person could determine whether the Vip3C variant was encompassed by the instant claims.

Written Description

Claims 49, 50, 55-58, 63, 64, 69-72, 80, 90, 95, 97 and 98 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Particularly, the Examiner contends that while the specification describes SEQ ID NO: 2, 11 and 32, one skilled in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Office Action at page 7. While Applicant maintains that the claims meet the requirements of §112, in the interest of advancing prosecution and without any intention to relinquish any scope of equivalents unforeseeable at the time of this amendment, claims 50, 55-57, 63, 64 and 69-72 have been canceled and claim 49 has been amended. Applicant respectfully submits that the cancellation of claims 50, 55-57, 63, 64, and 69-72 renders the rejection of these claims moot.

The instant claims define subject matter which is described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed subject matter at the time the application was filed.

The written description requirement of 35 U.S.C. §112, first paragraph, does not require a description of the complete structure of every species within a chemical genus. See Utter v. Hiraga, 845 F.2d 993, 998 (Fed. Cir. 1988) (“A specification may, within the meaning of 35 U.S.C. §112 ¶1, contain a written description of a broadly claimed invention without describing all species the claim encompasses.”).

The Federal Circuit has addressed the issue of what constitutes adequate written description. In Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316 (Fed. Cir. 2002), the court

adopted a portion of the Guidelines proffered by the Patent and Trademark Office (USPTO). The court stated that:

The written description requirement can be met by “showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Enzo Biochem, 296 F.3d at 1324 (citations omitted).

The subject matter encompassed by claims 49 and the dependent claims thereof is disclosed by the specification. In the instant case, the complete structure of the insecticidal toxin of SEQ ID NO: 2 has been described, and the genus limited to a toxin which is active against European corn borer (ECB) having at least 97% sequence identity to SEQ ID NO: 2 and wherein the C-terminus of said toxin comprises amino acids 661-788 of SEQ ID NO: 2. The specification describes two additional toxin species by disclosing the complete structure of SEQ ID NO: 11 and SEQ ID NO: 32. The specification describes how to make the toxin of SEQ ID NO: 11 by moving amino acids 661-788 of SEQ ID NO: 2 (the ECB-active C-terminal domain) to a nonECB-active Vip3 (e.g. Vip3A) and demonstrating that the resulting toxin now has ECB activity in addition to other lepidopteran insects (See Table 10 at paragraph [00184]). The specification describes how to isolate the toxin of SEQ ID NO: 32 from *Bacillus*. It would be routine for the skilled person to determine that SEQ ID NO: 11 and SEQ ID NO: 32 have 97% and 99% sequence identity to SEQ ID NO: 2, respectively, using the teaching of the instant application as well as that which was routine in the art at the time the application was filed. The specification also describes the structural feature of SEQ ID NO: 2, SEQ ID NO: 11 and SEQ ID NO: 32 that is correlated with functionality against ECB, which is amino acids 661-788 of SEQ ID NO: 2 (See Example 9). The specification also describes that in addition to European corn borer, the claimed toxin has activity against other lepidopteran insects (See Example 13).

The Examiner contends that Selvapandiyan *et al.* teach that Vip3 toxins that differ by three amino acids have different insect specificities and therefore, without guidance on structure to function of insecticidal toxins, one skilled in the art would not know which residues of the sequence are essential for function/activity of the toxin variants. Applicant respectfully disagrees

with the Examiner for the following reasons. First, the instant claims require that the toxin variants comprise amino acids 661-788 of SEQ ID NO: 2 at the C-terminus, which is identified to the skilled person as being the essential structural feature providing functionality of the toxin against ECB. Second, it is not clear from Selvapandiyan *et al.*, as the Examiner asserts, that the three amino acid differences between the Vip3S and the Vip3A(b) sequence are responsible for the lack of activity of Vip3S against black cutworm. On page 5857, column 2, last paragraph, Selvapandiyan *et al.* state, “*At present, it is difficult to understand the reasons for the observed lack of insecticidal activity against A. ipsilon by VIP described here. Is it due to diversity in A. ipsilon, or are the three different amino acid residues in VIP critical for toxicity?*” Applicant respectfully submits that given the inconclusive results, Selvapandiyan *et al.* has no bearing on whether the present claims meet the written description requirement.

Applicant respectfully submits that the present claims specifically define the claimed genus through the recitation of chemical structure and function and that the specification reasonably describes their correlation. Applicant respectfully submits that one skilled in the art would recognize that, given the sequence information of SEQ ID NO: 2, SEQ ID NO: 11 and SEQ ID NO: 32, the teaching that amino acids 661-788 of SEQ ID NO: 2, which is comprised in SEQ ID NO: 2, SEQ ID NO: 11 and SEQ ID NO: 32, are responsible for functionality against European corn borer, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed toxins at the time of filing of this application.

In view of the above amendments and remarks, Applicant respectfully requests that the rejection of claims 49, 58, 80, 90, 95, 97 and 98 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 49, 70, 80, 90, 95, 97 and 98 stand rejected under 35 U.S.C. §102(e) as being anticipated by Schnepf *et al.* (US Patent 6,369,213). The Office asserts that Schnepf *et al.* disclose a toxin (SEQ ID NO: 82) produced by expression of a nucleic acid (SEQ ID NO: 83) with 92.9% identity to SEQ ID NO: 1 of the instant application. Claim 70 has been canceled rendering the rejection of this claim moot.

Section 102(e) requires the prior art invention to be described in a U.S. patent, invented by another; and filed before the date of the applicant's invention. Applicant respectfully submits that Schnepf *et al.* do not describe the instant invention.

Claim 49 as amended, and the claims dependent therefrom, require that the isolated toxin encompassed by the claims comprises an amino acid sequence that has at least 97% identity with SEQ ID NO: 2 over the entire length of the amino acid sequence, comprises at its C-terminus amino acids 661-788 of SEQ ID NO: 2 and have activity against European corn borer.

The toxin of Schnepf *et al.* (SEQ ID NO: 82), called 86BB1(c), has only 90% sequence identity to SEQ ID NO: 2 of the instant application (See Exhibit B enclosed herewith), does not comprise amino acids 661-788 of SEQ ID NO: 2 at its C-terminus and there is no indication that the 86BB1(c) toxin is active against European corn borer.

In view of the above amendments and Applicant's remarks, Applicant respectfully submits that Schnepf *et al.* can not anticipate Applicant's invention and therefore requests that the rejection of claims 49, 80, 90, 95, 97 and 98 under 35 U.S.C. § 102(e) be withdrawn.

Rejection under 35 U.S.C. § 102/35 U.S.C. § 103

Claims 71 and 72 stand rejected under 35 U.S.C. § 102(e) as anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Schnepf *et al.* (US Patent 6,369,213). Claims 71 and 72 have been canceled rendering rejection to these claims moot.

Rejection under 35 U.S.C. § 103

Claims 49, 55-58, 70, 80, 90, 95, 97 and 98 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Schnepf *et al.* (US Patent 6,369,213) in view of Stemmer *et al.* (US Patent 6,500,617). The Examiner asserts that Schnepf *et al.* teach a toxin (SEQ ID NO: 82) with 90.6% identity to SEQ ID NO: 2. The Examiner acknowledges that Schnepf *et al.* do not disclose a toxin with 91%, 95%, 97% or 99% identity to SEQ ID NO: 2. The Examiner further asserts that Stemmer *et al.* teach a method of making variants in pest resistance genes. The Examiner suggests that at the time the instant application was made, it would have been obvious to one of ordinary skill in the art to modify the toxin taught by Schnepf *et al.* to use the method of

Stemmer *et al.* to make variants of their toxin, thereby making a toxin with 91%, 95%, 97% or 99% identity to SEQ ID NO: 2. Claims 55-57 and 70 have been canceled rendering the rejection to these claims moot. As to remaining claims, Applicant respectfully disagrees that Schnepf *et al.* in view of Stemmer *et al.* makes obvious the instant invention.

Claim 49 as amended, and the claims dependent therefrom, require that the isolated toxin encompassed by the claims comprises an amino acid sequence that has at least 97% identity with SEQ ID NO: 2 over the entire length of the amino acid sequence, comprises at the C-terminus amino acids 661-788 of SEQ ID NO: 2 and have activity against European corn borer.

It is well settled that in order to support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See In re Lowry, 32 F.3d 1579, 1582 (Fed. Cir. 1994). In addition, the record must provide evidence that those of skill in the art would have had a reasonable expectation of success in doing so. See In re Dow Chemical Co., 837 F.2d 469, 473 (Fed. Cir. 1988).

Schnepf *et al.* do not disclose or suggest the toxin of amended claim 49. The toxin of Schnepf *et al.* (86BB1(c); SEQ ID NO: 82) does not have 97% sequence identity to SEQ ID NO: 2; does not comprise at its C-terminus amino acids 661-788 of SEQ ID NO: 2; nor is it active against European corn borer. Schnepf *et al.* do not disclose or remotely suggest that the ECB functional domain of SEQ ID NO: 2 of the instant application comprises amino acids 661-788 of SEQ ID NO: 2. An alignment (Exhibit B) of the 86BB1(c) toxin of Schnepf *et al.* with SEQ ID NO: 2 of the instant application shows that the C-terminal domain of 86BB1(c) that aligns with amino acids 661-788 of SEQ ID NO: 2 has very little sequence identity with SEQ ID NO: 2.

Although Stemmer *et al.* suggest a general method of making variants of pest resistance genes, they do not disclose or suggest the instant invention. There is no suggestion in Stemmer *et al.* to target the C-terminal region of a Vip3 protein for shuffling in order to create a toxin active against European corn borer. Stemmer's method suggests shuffling the entire pest resistance gene in order to arrive at a variant toxin.

Applicant respectfully submits that it would not have been obvious to the skilled person to modify the toxin taught by Schnepf *et al.* using the method taught by Stemmer *et al.* to arrive at the instant invention. The skilled person had no way of knowing that the C-terminal domain of Vip3C was responsible for European corn borer activity and therefore the skilled person would have no expectation whatsoever at successfully arriving at a Vip3C variant having at least 97%

identity to SEQ ID NO: 2 over the entire length of the amino acid sequence, comprising at its C-terminus amino acids 661-788 of SEQ ID NO: 2 and having activity against European corn borer.

In view of the above described amendments and Applicant's remarks, Applicant respectfully submits that Schnepf *et al.* and Stemmer *et al.* either alone or in combination do make obvious the claimed invention and request that the rejection of claims 49, 58, 80, 90, 95, 97 and 98 under 35 U.S.C. §103(a) be withdrawn.

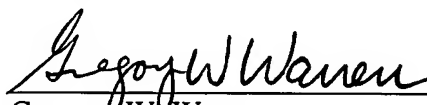
CONCLUSION

Applicant respectfully submits that the pending claims are in condition for allowance.
Applicant respectfully solicit a Notice of Allowance to that effect.

Should the Examiner wish to discuss any outstanding matter, the Examiner is invited to telephone the undersigned agent.

Respectfully submitted,

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